REMARKS

As of the Office Action, claims 1, 2, 4-31, 33-59, 61-85, 87-109, and 114-120 were pending in the application and stand rejected. With this reply claims 1, 27, 31, 55, 59, 80 , 85, and 105 are amended, while claims 22-24, 26, 50-52, 54, 77-79, 81, 103-104, and 106 are cancelled. Upon entry of the amendments, claims 1, 2, 4-21, 25, 27-31, 33-49, 53, 55-59, 61-76, 80, 82-85, 87-102, 105, 107-109, and 114-120 remain pending in the application.

Support for the claim amendments is found in the specification as originally filed. In particular, the main claims have been amended to recite subject matter found in some of their dependent claims. No new matter is added, Applicants respectfully request entry of the amendments.

FINALITY OF THE LAST OFFICE ACTION

Applicants thank the Examiner for removing the finality of the last rejection and issuing another non-final rejection. Applicants respectfully request reconsideration in light of the claim amendments and the following discussion, which addresses the new grounds of rejection.

REJECTION UNDER 35 U.S.C. § 112

Claims 1, 2, 4-12, 19, 22-31, 33-40, 45-47, 50-59, 61-74, 77-85, 87-100, 103-109, and 114 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse the rejection as applied to the amended claims and request reconsideration.

The written description requirement is satisfied when all of the claim elements are found in the specification and described as recited in the claims. The requirement is used to prohibit the introduction of "new matter" into an application during prosecution, in order to enforce the statutory requirement that a patent may be acquired only for an invention the applicant has actually disclosed at the time of filing. The cases have held that if the disclosure of an invention in a specification is sufficient to demonstrate that the inventors were "in possession" of the invention at the time of filing, the requirement is satisfied.

Contrary to the assertion in the Office Action, the claims are supported by the specification, which clearly shows the inventors were in the possession of the claimed invention. The identity of the cores and the coatings in various embodiments are described for example in

paragraphs [0013] – [0015]. Dissolution profiles of the tablets are described in paragraph [0013], [0030], and [0031] for example. Paragraph [0025] clarifies that tablet cores are coated with a coating designed to achieve an extended release of metformin. The specification makes it clear that the coated tablet cores achieve the release profiles recited in the claims. In particular, paragraph [0025] discloses that coatings with the recited ratio of water insoluble polymer; water soluble polymer; and plasticizer are permeable to metformin and free of pore forming agents. The cores, coatings, and release profiles described in the specification are recited in the claims. Applicants respectfully submit that the claims are thus supported by the written description and respectfully request the § 112 rejection be withdrawn.

REJECTION UNDER 35 U.S.C. § 102

Claims 1, 2, 4-13, 15, 17-19, 22, and 28-30 stand rejected under 35 U.S.C. § 102(b) as anticipated by U.S. Patent 5,955,106, Moeckel et al., issued September 21, 1999 (hereinafter *Moeckel*) and U.S. Patent 6,099,859, Cheng et al., issued August 8, 2000 (hereinafter *Cheng*). Applicants traverse the rejections as applied to the amended claims and request reconsideration. As pertinent to the anticipation rejections over *Moeckel* and *Cheng*, Applicants have amended claim 1 to incorporate claim 23, which is not subject to either rejection. Because the subject matter of the amended claims is not disclosed in either of the references, Applicants respectfully request the anticipation rejection be withdrawn.

REJECTIONS UNDER 35 U.S.C. § 103

All of the pending claims (1, 2, 4-31, 33-59, 61-85, 87-109, and 114-20) stand rejected as obvious over *Moeckel* in view of U.S. Patent 5,472,712, Oshlack et al., issued December 5, 1995 (hereinafter *Oshlack*) and U.S. Patent Publication 2003/0021841A1, Matharu et al, published January 30, 2003 (hereinafter *Matharu*) and further in view of U.S. Patent 6,592,900B1, Bühler et al., issued July 15, 2003 (hereinafter *Bühler*) and Remington's Pharmaceutical Sciences 1990 18th Ed. Chpt. 89, p. 1637. Applicants respectfully traverse the rejection as applied to the amended claims and request reconsideration.

Claims 1, 31, 59, and 85 have been amended to recite that the metformin cores contain a non-hydrocolloid expanding agent. Claims 114-120 also recite cores containing a non-hydrocolloid expanding agent (crospovidone). This feature is not present in the combined

references; in fact *Moeckel* in combination with the other references teaches away from it. Reconsideration is respectfully requested in light of the following discussion.

In particular, *Moeckel* teaches that its cores have to contain a "retardant" to overcome disadvantages of prior art metformin tablets, as shown in the following citations from the reference (emphasis added throughout):

> The object of the invention was to provide an improved pharmaceutical composition for the active substance metformin. In particular the form of administration should contain the active substance metformin with a highest possible content of active substance and a retardant, the retardant causing a controlled release of the active substance. *Col. 1, lines 33-38*
>
> In the present case the object of the invention is achieved by providing high-dose pharmaceutical compositions containing metformin which contain a hydrocolloid-forming agent as a retardant . . . *Col. 2, lines 17-20*
>
> In addition it surprisingly turned out that the use of a hydrocolloid-forming agent enabled for the first time the known poor compressibility of metformin to be brought under control in a technically satisfactory manner. *Col. 2, lines 58-61*
>
> Within the sense of the invention the standard hydrophilic gel forming agents are suitable as hydrocolloid-forming agents or as hydrophilic swelling substances such as for example cellulose derivatives, dextrins, starch, carbohydrate-based polymers, natural or hydrophilic gums, xanthanes, alginates, gelatin, polyacrylic acid, polyvinyl alcohol or polyvinylpyrrolidone. In the case of the cellulose derivatives the alkyl or hydroxyalkyl cellulose derivatives preferably come into consideration such as e.g. methyl cellulose, hydroxymethyl cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, methylhydroxyethyl cellulose, methylhydroxypropyl cellulose or sodium carboxymethyl cellulose. *Col. 3, lines 20-33*
>
> The use of hydrocolloid-forming agents as retardants is based on the property of the hydrocolloid-forming agents to swell and form a gel matrix when they are contacted with a release medium or digestive juices which erodes to release the active substance. *Col. 3, lines 41-45*

These passages establish that the *Moeckel* cores are required to have a component that retards release of the metformin. On the other hand, Applicants' claims recite cores that contain an expanding agent. As explained in paragraph [0023], the expanding agent of the claims acts as a disintegrant. Because the non-hydrocolloid expanding agents of the claims tend to act as

disintegrants, whereas the hydrocolloid forming agents of *Moeckel* react as a retardant to disintegration, *Moeckel* actually teaches away from the subject matter of the amended claims.

The secondary references do not provide the claim features missing from *Moeckel*. No matter what features of the secondary references are brought together by combining with *Moeckel*, there is still the teaching in *Moeckel* against using the non-hydrocolloid expanding agent of the claims. The secondary references do not overcome this teaching.

In particular, *Oshlack* is recited for teaching a coating of ethyl cellulose, plasticizer, and polyvinylpyrrolidone. Even if the reference thus suggests coatings like those recited in the claims, the reference still does not amount to a disclosure or motivation to use metformin cores having a non-hydrocolloid expanding agent as recited in the amended claims. As such, it does not overcome the teaching away by *Moeckel*.

Matharu discloses compressible cores containing metformin. But the reference teaches that the cores containing erodible component which is "a water loving soluble gelling agent" (See paragraph [0011]). This is still not a teaching of the non-hydrocolloid expanding agent of the cores, nor a teaching or motivation to use it at a level of 3 to 25% by weight. As such, Applicants submit that the *Matharu* reference by itself or in combination with the *Oshlack* reference does not overcome the teaching away by the *Moeckel* reference discussed above.

Further in this regard, attention is respectfully drawn to *Buhler*. At column 2, lines 41-47, the reference teaches that polyvinylpyrrolidone is soluble while crospovidone is insoluble. Soluble polyvinylpyrrolidone is a suitable "water loving water soluble/gellable agent" for use as a hydrophilic erodible component, according to *Matharu*. See *Matharu* at paragraph [0011]. In contrast, the insoluble crospovidone is an example of a non-hydrocolloid expanding agent as recited in the claims, as described in the current specification at paragraphs [0023] and [0033]. This establishes that the non-hydrocolloid expanding agent (e.g. crospovidone) of the claims is not suggested by *Matharu* in combination with *Moeckel* or the other secondary references. In particular, the secondary references are not sufficient to overcome the deficiencies and teaching away of *Moeckel* discussed above.

For these reasons, Applicants respectfully request that the obviousness rejection, as applied to the amended claims, be withdrawn.

The pending claims are also rejected as obvious over *Cheng* in view of the same secondary references. Applicants respectfully traverse the rejections as applied to the amended claims and request reconsideration.

As noted in previous prosecution, *Cheng* teaches away from the subject matter of the current claims. In particular, *Cheng* teaches metformin tablets with a coating that is impermeable to metformin. Thus, at column 4, lines 10-16, *Cheng* states:

> The homogenous core is coated with a semi-permeable membrane, preferably a modified polymeric membrane to form the controlled release tablet of the invention. The semi-permeable membrane is permeable to the passage of an external fluid such as water and a biological fluid and is impermeable to the passage of the anti-hyperglycemic drug in the core.

Any modification of *Cheng* to supply a permeable coating, as recited in the rejected claims, would change the mode of operation of the reference. For this reason, any such modification would not have been obvious to a person of skill in the art. Applicants further submit that the cited secondary references, discussed above, do not supply any motivation to modify *Cheng* to provide cores that are permeable to metformin, as recited in the claims. For these reasons, Applicants respectfully request that the obviousness rejection over *Cheng* be withdrawn.

CLAIMS 114-120

Claims 114-120 are not amended, but distinguish over the cited references for the reasons discussed above. These claims all recite cores containing crospovidone which, as developed above, is a non-hydrocolloid expanding agent not suggested by the references. The claims also recite coatings permeable to metformin; *Cheng* teaches away from the use of such coating.

For these reasons, Applicants request reconsideration and withdrawal of the rejections of claims 114-120.

CONCLUSION

Applicants submit that claims 1, 2, 4-21, 25, 27-31, 33-49, 53, 55-59, 61-76, 80, 82-85, 87-102, 105, 107-109, and 114-120 are in an allowable condition and respectfully request a Notice of Allowance. The Examiner is invited to telephone the undersigned if that would be helpful to resolving any issues.

Respectfully submitted,

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